REMARKS

Claims 1-16 were at issue. Claims 1-16 were rejected. The Examiner made the following rejections:

(1) The Examiner requests the Applicants file a new declaration that is compliant with 37 CFR 1.67(a).

(2) The Examiner requests the Applicants reference their priority claim in the first sentence of the specification pursuant to 37 CFR 1.78.

(3) The Examiner objects to informalities in the Specification.

(4) The Examiner objects to an informality in Claim 1.

(5) Claims 1-16 are rejected under 35 U.S.C. (first paragraph).

(6) Claims 1-16 are rejected under 35 U.S.C. (second paragraph).

The Applicants believe the present amendments and the following remarks traverse the Examiner's rejection of the pending claims. These remarks are presented in the same order as they appear above.

1. Applicants Provide New Declarations

The Applicants have attached new declarations, in compliance with 37 CFR 1.67(a), wherein the Applicants claim priority to the following two provisional applications: i) 60/141,156 (filed June 23, 1999) and ii) 60/199,699 (filed April 26, 2000).

2. Applicants Are Compliant With 37 CFR 1.78

The Applicants have inserted a sentence (as the first sentence of the specification) reciting a priority claim, under 35 U.S.C. 119(e), to two previously filed patent provisional patent applications.

3. The Applicants Have Amended The Specification

The Applicants have amended the specification to harmonize reference, in the specification, to selected re-formatted figures.[1] No new matter was added by the amendments to the description(s) of these re-formatted figures.

The Applicants have deleted, from the specification, the embedded hyperlinks identified by the Examiner. Applicants note that these hyperlinks were originally provided for the Examiner's convenience and *are not* needed to enable the invention as claimed.

Applicants have also amended portions of the specification to correct misspellings. Finally, Applicants have amended the definition of "binding interaction" (see, line 24 on page 10 of the application as filed) in order to clarify the meaning of the same.

4. The Applicants Have Amended The Claims

The Applicants have amended claim 1 to address the informality cited by the Examiner. The Applicants, however, respectfully note well settled patent law supports the proposition that the claims are to read in view of the specification. See, *General Foods Corp v. Studiengesellschaft Kohle mbH*, 972 F.2d 1272, 1274 (Fed. Cir. 1992). The specification clearly identifies "Mod5p" as a protein. For example on line 1 on page 18, of the application as filed, Applicants state that "[t]he *Saccharomyces cerevisiae* protein Mod5p catalyzes the addition of an isopentenyl group to adenosine. . .". Therefore, further designation of Mod5p as a protein, in the claims, is unnecessary. However, in order to further the Applicants' business interest and without acquiescing to the Examiner's argument or waiving their right to prosecute claim as filed (or claims similar thereto), Applicants have amended claim 1 to reenforce the designation of "Mod5p" as a protein.

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[1] See, Figs. 2, 3, and 5. Please note that a finalized figure, satisfying the standards of "Formal Drawings", is being filed along with the instant Response.

5. The Claims Are Enabled

A. The Examiner Fails To Make A *Prima Facie* Case.

The Examiner rejects claims 1-16 under 35 U.S.C. 112, first paragraph. Specifically, the Examiner alleges the Specification does not allow any person skilled in the art to, "determine the meaning of the comparisons of treated to untreated portions and thus would not be able to make and / or use the claimed methods." See, Office Action, page 4. The Examiner is reminded that, "it is incumbent upon the Patent Office, whenever a rejection on [the basis of lack of enablement] is made, to explain why it doubts the truth or accuracy of any statement in supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." *In re Marzocchi*, 169 USPQ 367, 370 (CCPA 1971).

In view of *In re Marzocchi*, the Examiner fails to provide explanation, evidence, or reasoning as to how the Applicants' specification fails to enable the scope of the invention as claimed. Instead, the Examiner summarily states that a preamble reciting a "method" (without further qualification) is insufficient to satisfy 35 U.S.C. §112, first paragraph. The Applicants respectfully submit the Examiner has not considered and / or discussed the adequacy of the teachings provided in the application as filed (*vis-a-vis* the recitation of a "method" in the preamble) and, therefore, has failed to make a *prima facie* case.

However, in order to further the Applicants' business interest and without acquiescing to the Examiner's argument or waiving their right to prosecute claim as filed (or claims similar thereto), Applicants have amended the preamble of all pending independent claims to either recite: i) "a method for screening compounds that are agonistic or antagonistic to the melvalonate pathway in sterol synthesis" (see, claims 1, 4, 7, 10, 12, 14, and 17) or ii) "a method of screening for overexpressed yeast genes" (see, claim 20). The Applicants respectfully submit the instant amendments, to the preambles enumerated above, traverse the Examiner's rejection and therefore this rejection, under 35 U.S.C. §112, first paragraph, should be withdrawn.

B. The Claims Are Definite

The Examiner is reminded that "[c]laims of a patent application *are to be construed in the light of the specification* and the understanding thereof by those skilled in that art to whom they are addressed'." *Application of Salem*, 553 F.2d 676, 683, 193 USPQ 513 (CCPA 1977) (quoting *In re Myers*, 410 F.2d 420, 425 (CCPA 1969) with emphasis added in *Salem*). Furthermore, "[t]he patent law 'allows the inventor to be his own lexicographer,' " *Loctite Corp. v. Ultraseal Ltd.*, 781 F.2d 861, 867, 228 USPQ 90, 93 (Fed. Cir. 1985) (quoting *Autogiro Co. of America v. United States*, 384 F.2d 391, 397, 155 USPQ 697, 702 (Ct. Cl. 1976)). The Applicants, therefore, are free to introduce any descriptive term or phase into the claims so long as these descriptors are adequately defined in the Specification.

i. Homolog Is Defined In The Specification

The Examiner states the pending claims, rejected under 35 U.S.C. §112, second paragraph as, are "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." See, Office Action, Page 4. The Applicants respectful submit the Examiner need look no further than the specification of the application as filed to find an explicit definition for a term in dispute.

However, in order to further the Applicants' business interest and without acquiescing to the Examiner's argument or waiving their right to prosecute claim as filed (or claims similar thereto), Applicants have amended the pending claims such only (new) claim 17 recites, in part, a homolog of Mod5p.

ii. Applicants Have Elaborated On The Steps In The Claimed Methods

The following three statements represent the balance of the grounds upon which the Examiner rejects (under 35 U.S.C. §112, second paragraph) the pending claims:

1. In claims 1, 4, 7, 10, 12 and 14 it is unclear if the portions are actually portions of modified yeast cells and if both treated and untreated portions are exposed to the growth media.

2. In claims 2, 5 and 8 it is unclear if the modified yeast cells are being measured for growth.

3. There is insufficient antecedent basis for the term "yeast cells" in claims 2, 5, and 8.

4. In claims 3, 6, 9, 11, 13 and 15 it is unclear what property is being compared. The Applicants assert the claims as filed are definite and satisfy 35 U.S.C. §112, second paragraph. However, in order to further the Applicants' business interest and without acquiescing to the Examiner's argument or waiving their right to prosecute claim as filed (or claims similar thereto), Applicants have amended all but claim 16 to more explicitly recite the sequence of the steps comprising the methods as claim. Applicants note that no new matter was added by way of these amendments and respectfully request the Examiner withdraw all pending rejections under 35 U.S.C. §112, second paragraph.

iii. Applicants Have Added New Claims

The Applicants have added new claims in the instant Office Action Response. One of these claims, claim 20, recites, " [a] method for screening for overexpressed genes." Applicants note that this new claim finds explicit support in the specification of the application as filed. Specifically, the Examiner is directed to pages 17 - 19, and lines 6 - 12 of page 29 for expository support of the embodiment of the invention as claimed in claim 20.

CONCLUSION

The Applicants believe the arguments and claim amendments set forth above traverse the Examiner's rejections and, therefore, request that all grounds for rejection be withdrawn. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, the Applicants encourage the Examiner to call the undersigned collect at 617.252.3353.

Dated: September 11, 2002

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APPENDIX I
MARKED-UP VERSION OF REWRITTEN CLAIMS
PURSUANT TO 37 CFR § 1.121 (c)(1)(ii)

The following claims were amended in the instant correspondence:

(Amended) 1. A method for screening compounds that are agonistic or antagonistic to the melvalonate pathway in sterol synthesis, comprising:

a) providing: i) a test compound, ii) a growth media formulated to allow scoring of nonsense suppression in yeast, and iii) modified yeast cells derived from wild type yeast cells, wherein said modified yeast cells express reduced cytosolic levels of Mod5p, wherein the "p" in "Mod5p" refers to a polypeptide, [or its homolog] as compared to said wild type yeast cells, and wherein said modified yeast cells comprise a gene with a nonsense mutation and a suppressor tRNA gene coding for a tRNA modified with isopentenyl adenosine by Mod5p [or its homolog];

b) mixing said growth media and said modified yeast cells to form an untreated modified yeast cell mixture;

[b)]c) adding [exposing a portion] an aliquot of said untreated modified yeast cell[s] mixture to said test compound [and said growth media to create a treated portion and an untreated portion] thereby creating a treated modified yeast cell mixture; and

[c)] d) measuring [for growth of said treated portion] the growth of said modified yeast cells in said treated modified yeast cell mixture.

(Amended) 2. The method of Claim 1, wherein said measuring of step [(c)] d) comprises examining the color of said modified yeast cells [of said treated portion] within said treated modified yeast cell mixture.

(Amended) 3. The method of Claim 1, wherein said measuring of step [(c)] d) comprises comparing [said treated portion with said untreated portion, wherein said untreated portion is exposed to said growth media in the absence of said test compound] the growth and color of the modified yeast cells within said treated modified yeast cell mixture with the growth and color of the modified yeast cells within said untreated yeast cell mixture.

(Amended) 4. A method for screening compounds that are agonistic or antagonistic to the melvalonate pathway in sterol synthesis, comprising:

a) providing: i) a test compound, ii) a growth media lacking adenine, and iii) modified yeast cells derived from wild type yeast cells, wherein said modified yeast cells express reduced cytosolic levels of Mod5p as compared to said wild type yeast cells, and wherein said modified yeast cells comprise an *ADE2* gene having a nonsense mutation and a gene coding for a nonsense suppressor tRNA;

b) mixing said growth media and said modified yeast cells to form an untreated modified yeast cell mixture;

[(b)] c) adding [exposing a portion] an aliquot of said untreated modified yeast cell[s] mixture to said test compound [and said growth media to create a treated portion and an untreated portion] thereby creating a treated modified yeast cell mixture; and

[(c)] d) measuring [for growth of said treated portion] the growth of said modified yeast cells in said treated modified yeast cell mixture.

(Amended) 5. The method of Claim 4, wherein said measuring of step [(c)] d) comprises examining the color of said modified yeast cells [of said treated portion] within said treated modified yeast cell mixture.

(Amended) 6. The method of Claim 4, wherein said measuring of step [(c)] d) comprises comparing [said treated portion with said untreated portion, wherein said untreated portion is exposed to said growth media in the absence of said test compound] the growth and color of the modified yeast cells within said treated modified yeast cell mixture with the growth and color of the modified yeast cells within said untreated yeast cell mixture.

(Amended) 7. A method for screening compounds that are agonistic or antagonistic to the melvalonate pathway in sterol synthesis, comprising:

a) providing: i) a test compound, ii) a growth media lacking adenine, and iii) modified yeast cells derived from wild type yeast cells, wherein said modified yeast cells express reduced cytosolic levels of Mod5p as compared to said wild type yeast

cells, and wherein said modified yeast cells comprise an *ADE2* gene having a nonsense mutation and a *SUP7* gene coding for a tRNA;

b) mixing said growth media and said modified yeast cells to form an untreated modified yeast cell mixture;

[(b)]c) adding [exposing a portion] an aliquot of said untreated modified yeast cell[s] mixture to said test compound [and said growth media to create a treated portion and an untreated portion] thereby creating a treated modified yeast cell mixture; and

[(c)] d) measuring [for growth of said treated portion] the growth of said modified yeast cells in said treated modified yeast cell mixture.

(Amended) 8. The method of Claim 7, wherein said measuring of step [(c)] d) comprises examining the color of said modified yeast cells [of said treated portion] within said treated modified yeast cell mixture.

(Amended) 9. The method of Claim 7, wherein said measuring of step [(c)] d) comprises comparing [said treated portion with said untreated portion, wherein said untreated portion is exposed to said growth media in the absence of said test compound] the growth and color of the modified yeast cells within said treated modified yeast cell mixture with the growth and color of the modified yeast cells within said untreated yeast cell mixture.

(Amended) 10. A method for screening compounds that are agonistic or antagonistic to the melvalonate pathway in sterol synthesis, comprising:

a) providing: i) a test compound, ii) a growth media lacking arginine and [comprising] containing a canavanine salt, and iii) modified yeast cells derived from wild type yeast cells, wherein said modified yeast cells express reduced cytosolic levels of Mod5p as compared to said wild type yeast cells, and wherein said modified yeast cells comprise a *CAN1* gene having a nonsense mutation and a gene coding for a nonsense suppressor tRNA;

b) mixing said growth media and said modified yeast cells to form an untreated modified yeast cell mixture;

[b)]c) adding [exposing a portion] an aliquot of said untreated modified yeast cell[s] mixture to said test compound [and said growth media to create a treated portion and an untreated portion] thereby creating a treated modified yeast cell mixture; and

[c)] d) measuring [for growth of said treated portion] the growth of said modified yeast cells in said treated modified yeast cell mixture.

(Amended) 11. The method of Claim 10, wherein said measuring of step [(c)] d) comprises comparing [said treated portion with said untreated portion, wherein said untreated portion is exposed to said growth media in the absence of said test compound] the growth and color of the modified yeast cells within said treated modified yeast cell mixture with the growth and color of the modified yeast cells within said untreated yeast cell mixture.

(Amended) 12. A method for screening compounds that are agonistic or antagonistic to the melvalonate pathway in sterol synthesis, comprising:

a) providing: i) a test compound, ii) a growth media lacking arginine and [comprising] containing a canavanine salt, and iii) modified yeast cells derived from wild type yeast cells, wherein said modified yeast cells express reduced cytosolic levels of Mod5p as compared to said wild type yeast cells, and wherein said modified yeast cells comprise a *CAN1* gene having a nonsense mutation and a *SUP7* gene coding for a tRNA;

b) mixing said growth media and said modified yeast cells to form an untreated modified yeast cell mixture;

[b)]c) adding [exposing a portion] an aliquot of said untreated modified yeast cell[s] mixture to said test compound [and said growth media to create a treated portion and an untreated portion] thereby creating a treated modified yeast cell mixture; and

[c)] d) measuring [for growth of said treated portion] the growth of said modified yeast cells in said treated modified yeast cell mixture.

(Amended) 13. The method of Claim 12, wherein said measuring of step [(c)] d) comprises comparing [said treated portion with said untreated portion, wherein said untreated portion is exposed to said growth media in the absence of said test compound] the growth and

color of the modified yeast cells within said treated modified yeast cell mixture with the growth and color of the modified yeast cells within said untreated yeast cell mixture.

(Amended) 14. A method for screening compounds that are agonistic or antagonistic to the melvalonate pathway in sterol synthesis, comprising:

a) providing: i) a test compound, ii) a growth media lacking lysine, and iii) modified yeast cells derived from wild type yeast cells, wherein said modified yeast cells express reduced cytosolic levels of Mod5p as compared to said wild type yeast cells, and wherein said modified yeast cells comprise a *LYS2* gene having a nonsense mutation and a gene coding for a nonsense suppressor tRNA;

b) mixing said growth media and said modified yeast cells to form an untreated modified yeast cell mixture;

[b)]c) adding [exposing a portion] an aliquot of said untreated modified yeast cell[s] mixture to said test compound [and said growth media to create a treated portion and an untreated portion] thereby creating a treated modified yeast cell mixture; and

[c)] d) measuring [for growth of said treated portion] the growth of said modified yeast cells in said treated modified yeast cell mixture.

(Amended) 15. The method of Claim 14, wherein said measuring of step [(c)] d) comprises comparing [said treated portion with said untreated portion, wherein said untreated portion is exposed to said growth media in the absence of said test compound] the growth and color of the modified yeast cells within said treated modified yeast cell mixture with the growth and color of the modified yeast cells within said untreated yeast cell mixture.

(New) 17. A method for screening compounds that are agonistic or antagonistic to the melvalonate pathway in sterol synthesis, comprising:

a) providing: i) a test compound, ii) a growth media formulated to allow scoring of nonsense suppression in yeast, and iii) modified yeast cells derived from wild type yeast cells, wherein said modified yeast cells express reduced cytosolic levels of Mod5p or its homolog as compared to said wild type yeast cells, and wherein said

modified yeast cells comprise a gene with a nonsense mutation and a suppressor tRNA gene coding for a tRNA modified with isopentenyl adenosine by Mod5 or its homolog;

b) mixing said growth media and said modified yeast cells to form an untreated modified yeast cell mixture;

c) adding an aliquot of said untreated modified yeast cell mixture to said test compound thereby creating a treated modified yeast cell mixture; and

d) measuring the growth of said modified yeast cells in said treated modified yeast cell mixture.

(New) 18. The method of Claim 17, wherein said measuring of step d) comprises examining the color of said modified yeast cells within said treated modified yeast cell mixture.

(New) 19. The method of Claim 17, wherein said measuring of step d) comprises comparing the growth and color of the modified yeast cells within said treated modified yeast cell mixture with the growth and color of the modified yeast cells within said untreated yeast cell mixture.

(New) 20. A method for screening for overexpressed genes, comprising:

a) providing: i) an overexpressed yeast gene wherein said overexpression alters the flux in the melvalonate pathway in sterol synthesis, ii) a growth media formulated to allow scoring of nonsense suppression in yeast, and iii) modified yeast cells derived from wild type yeast cells, wherein said modified yeast cells express reduced cytosolic levels of Mod5p as compared to said wild type yeast cells, and wherein said modified yeast cells comprise a gene with a nonsense mutation and a suppressor tRNA gene coding for a tRNA modified with isopentenyl adenosine by Mod5p;

b) mixing said growth media and said modified yeast cells to form an untreated modified yeast cell mixture;

c) adding an aliquot of said untreated modified yeast cell mixture with said overexpressed gene thereby creating an overexpressed gene treated mixture of modified yeast cells; and

d) measuring the growth of said overexpressed gene treated mixture of modified yeast cells.

(New) 21. The method, as claimed in claim 20, wherein said overexpressed gene is a yeast gene.

Appendix III
MARKED-UP VERSION OF REWRITTEN PARAGRAPHS
PURSUANT TO 37 C.F.R. § 1.121(b)(1)(iii)

1. On page 1 of the application as filed, after the "Title Of The Invention", the following paragraph was inserted:

PRIORITY

This application for patent under 35 U.S.C. 111(a) claims priority, under 35 U.S.C. § 119(e), to Provisional Applications Serial Numbers **60/141,156 (filed on 06/23/99) and 60/199,699 (filed on 04/26/00)**; wherein said Provisional Applications were filed under 35 U.S.C. 111(b).

2. On page 1 of the application as filed, starting on line 4 (just before the paragraph beginning: "This invention was made on part with government support under grants. . .") the following paragraph was inserted:

STATEMENT REGARDING FEDERAL SPONSORSHIP

3. In the specification, the paragraph beginning on line 12 of page 5 was modified as follows:

- -The present invention contemplates a composition comprising yeast with the relevant genotype of: *SUP7 ade2-1 can1-100 leu2-3 mod5-M2* and designated ALB1. The present invention further contemplates a composition wherein the yeast ALB1 is a strain of *Saccharomyces cerevisiae*. Still further, the present invention contemplates a composition comprising yeast with the relevant genotype of: *SUP7 can1-100 ade2-1 leu2-3 mod5::TRP1 ura3-1::MOD5* and designated ALB8. Even still further, the present invention contemplates a composition wherein the yeast ALB8 is a strain of *Saccharomyces cerevisiae*. Even further still, the present invention contemplates a composition comprising the yeast strain ALB1 wherein the genotype further comprises: *MATα mod5-M2 SUP7 ade2-1 can1-100 leu2-3, -112 lys1-1 lys2-1 trp1 ura3-1*. Even still further, the present invention contemplates a composition wherein the yeast ALB1 is a strain of [*Sacchoromyces*] *Saccharomyces cerevisiae*. Even further still, the present invention contemplates a composition comprising yeast with the relevant

genotype of:: *MATα SUP7 can1-100 ade2-1 leu2-3, -112 lys1-1 lys2-1 trp1 mod5::TRP1 ura3-1::MOD5* and designated ALB8. Even further still, the present invention contemplates a composition of claim 7 wherein the yeast is [*Sacchoromyces*] *Saccharomyces* cerevisiae.- -

4. On page eight of the application as filed, please the following paragraphs (beginning on line 4 and ending on line 15) were deleted:

[Figure 2 shows the level of isopentenylated tRNA found in ALB1 over-expressing *ERG20* is substantially reduced.

A. Low molecular weight RNA was prepared from ALB1 (*mod5-M2*) with each of the candidate genes or vector alone, ALB8 (*MOD5*) or MD14A (*mod5-1*). The RNAs were resolved on polyacrylamide gels, transferred to membranes and probed with anti-isopentenyl adenosine antibody (upper panel) or radiolabeled oligonucleotide complementary to mature $tRNA^{Tyr}$ (lower panel).

B. The levels of isopentenyl adenosine tRNA found in ALB1 with each of the candidate genes or vector only or in the strain ALB8 or MD14A were assessed by densitometric analysis of two immunoblots and expressed as a fraction of the level found in the "vector" control. (A) membrane 1 values; (B) membrane 2 values; (C) average values.]

and the following paragraphs were inserted:

Figure 2A is an autoradiograph. Low molecular weight RNA was prepared from ALB1 (*mod5-M2*) with each of the candidate genes or vector alone, ALB8 (*MOD5*) or MD14A (*mod5-1*). The RNAs were resolved on polyacrylamide gels, transferred to membranes and probed with anti-isopentenyl adenosine antibody (upper panel) or radiolabeled oligonucleotide complementary to mature $tRNA^{Tyr}$ (lower panel). This autoradiograph shows the level of isopentenylated tRNA found in ALB1 over-expressing *ERG20* is substantially reduced.

Figure 2B is a graph. This graph presents data showing the levels of isopentenyl adenosine tRNA found in ALB1 with each of the candidate genes or vector only or in the strain ALB8 or MD14A that were assessed by densitometric analysis of two immunoblots and expressed as a fraction of the level found in the

"vector" control. (A) membrane 1 values; (B) membrane 2 values; (C) average values. These data are also consistent with the finding that the level of isopentenylated tRNA found in ALB1 over-expressing *ERG20* is substantially reduced.

5. On page eight of the application as filed, the following paragraph (beginning on line 16 and ending on line 17) was deleted:

[Figure 3 presents a model of competition between i^6A modification of tRNA and sterol biosynthesis.]

and the following paragraphs were inserted:

Figure 3A presents a model of competition between i^6A modification of tRNA and sterol biosynthesis.

Figure 3B presents another model of competition between i^6A modification of tRNA and sterol biosynthesis.

6. On page eight of the application as filed, please the following paragraph (beginning on line 22 and ending on line 25) was deleted:

[Figure 5 presents two yeast strains that present limited cytosolic levels of Mod5p. Cells with the mod5-M2KR6 allele (T8-ID with YCfmod5-M2KR6 as projected in Fig. 5) have a very small cytosolic pool of Mod5p and the cells are unable to grow in the absence of lysine.]

and the following paragraphs were inserted:

Figure 5A presents the growth characteristics for ALB1 cells and T8-1D cells (with YCfmod5-M2,KR6) under conditions of normal flux through the sterol biosynthesis pathway.

Figure 5B presents the growth characteristics for ALB1 cells and T8-1D cells (with YCfmod5-M2,KR6) under conditions such that flux through the sterol biosynthesis pathway is increased.

Figure 5C presents the growth characteristics for ALB1 cells and T8-1D cells (with YCfmod5-M2,KR6) under conditions such that flux through the sterol biosynthesis pathway is decreased.

7. In the specification, paragraphs beginning on line 23 of page 9 and ending on line 33 of page 9 were modified as follows:

- -Yeast strain "ALB1" is defined as a substantially pure population of yeast with the genotype of: *MATα mod5-M2 SUP7 ade2-1 can1-100 leu2-3, -112 lys1-1 lys2-1 trp1 ura3-1* and the relevant genotype of: *SUP7 ade2-1 can1-100 leu2-3-112 mod5-M2*. The yeast may be of the species [*Sacchoromyces*] Saccharomyces *cerevisiae.*

Yeast strain "ALB8" shall be defined as a substantially pure population of yeast with the genotype of:[:] *MATα SUP7 can1-100 ade2-1 leu2-3, -112 lys1-1 lys2-1 trp1 mod5::TRP1 ura3-1::MOD5*. The yeast may be of the species [*Sacchoromyces*] Saccharomyces *cerevisiae.*

Yeast strain "T8-1D" shall be defined as a substantially pure population of yeast with the genotype of:[:] *MATα SUP11 ade2-1 leu2-3, -112 mod5-1 lys2-1 his4-519 ura 3-1*. The yeast may be of the species [*Sacchoromyces*] Saccharomyces *cerevisiae.*- -

8. In the specification, the paragraph beginning on line 24 of page 10 was modified as follows:

- -The term "binding interaction" when used in relation to RNA shall be defined as the ability of two or more [proteins] macromolecules to bind to each other (*e.g.*, to produce an aggregate). The present invention makes no limit on the stringency of the binding interaction so long as the interaction can be detected by methods known to those practiced in the art (*e.g.*, by Western blot, coimmunoprecipitation, spectrophotometry, colorimetric assay, etc.).- -

9. In the specification, the paragraph beginning on line 18 of page 18 and ending on line 29 of page 18 was modified as follows:

ORF YDL219w is predicted to code for a 150 amino acid protein with no significant homology to any characterized protein. However two lines of evidence indicate that this protein may function in the translation process. First, the gene possesses an intron [(*Saccharomyces* Genome Database, http://genome-www.stanford.

edu/cgi-bin/dbrun)]. As introns are rare in yeast other than for approximately half of the genes encoding ribosomal proteins (Woolford and Warner, in "The molecular and cellular biology of the yeast *Saccharomyces*: Genomic dynamics, protein synthesis and energetics" eds. Broach, *et al.* [Cold Spring Harbor Lab Press, Plainview, NY] Vol. 1, pp. 587-626, 1991), the presence of the intron is suggestive of a role in translation. Second, Applicants show that over expression of YDL219w affects tRNA-mediated nonsense suppression.

10. In the specification, the paragraph beginning on line 6 of page 32 and ending on line 16 of page 32 was modified as follows:

Library plasmids were isolated from yeast by the method of Ward (Ward, "Single-step purification of shuttle vectors favor yeast for high frequency back-transformation into *E. coli*" *Nucleic Acids Res* 18:5319, 1990). DNAs were sequenced by either the chain termination method (Sanger, *et al.*, "DNA sequencing with chain-terminating inhibitors" *Proc Natl Acad Sci USA* 74:5463-5467, 1977) with Psychognosy Version 2.0 DNA Sequencing Kit (United States Biochemical) or by automated cycle sequencing performed in the Pennsylvania State University College of Medicine Macromolecular Core Facility. Nucleotide sequences were identified by a BLAST (Altschul, *et al.*, "Basic local alignment search tool" *J Mol Biol* 215:403-410, 1990) search at the *Saccharomyces* Genome Database BLAST server [(http://genome-www2.stanford.edu/cgi-bin/SGD/nph-blast2sgd/)].